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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,889	12/15/2003	Elias Georges	112418-147 and AUR-013US	5738

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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/736,889	GEORGES ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-108* is/are pending in the application.

4a) Of the above claim(s) *11, 13, 20-58, 67, 69, 75-108* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12,14-19,59-66,68 and 70-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12-15-04, 3-16-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I and species of fluorophores in the reply filed on 7/5/05 is acknowledged.

Applicants are also required to elect a single species from group a, and a single species from group b, in the event that applicants elect Group I. However, The Applicants did not meet the requirement and made no elections of these two species. During a telephone conversation with Mr. James Olesen on July 27, 2005, Applicants made election over telephone, breast cancer cell from group a, and modified LDL, in group b with traverse. Affirmation of this election must be made by Applicant in replying to this Office action.

Applicants argue in the response that there would be no serious burden on the examiner to search the claims of Group II along with the claims of elected group I, because group II is related to kits comprising a probe for the detection of vimentin.

These have been considered, but not found persuasive. The invention group I is a method for detecting vimentin in MDR, while group is a product comprising a probe for detection of vimentin.

According to MPEP ¶ 806.05(h), A product and a process of using the product can be shown to be distinct inventions if either or both of the following can be shown: (A) the process of using as claimed can be practiced with another materially different product; or (B) the product as claimed can be used in a materially different process. In this case, detecting MDR potential by comparing the level of vimentin protein can be practiced with another materially different product such as DNA probe for detecting the levels of mRNA. For these reasons, the group I and II are patentablely distinct inventions and the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made **FINAL.**

Claims 1-108 are pending. Claims 11, 13, 20-58, 67, 69, 75-108 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species and non-elected inventions. Claims 1-10, 12, 14-19, 59-66, 68, 70-74 are examined on the merits.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on Dec 15, 2004 and March 16, 2005 are considered by the examiner and initialed copy of the PTO-1449 is enclosed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1, 3-4, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Meschini et al., (Int, J. Cancer, Vol 87, page 615-628, 2000).

Claim 1 is drawn to a method for detecting MDR or MDR potential in a test neoplastic cells comprising measuring a level of cell surface-expressed vimentin protein in the test neoplastic cells and comparing the level of cell surface-expressed vimentin protein in the test neoplastic cell to the level of cell surface-expressed vimentin in a nonresistant neoplastic cell. Claims 3-4 are further drawn to claim 1, wherein measuring the levels of cell surface expression vimentin in the test neoplastic cells by vimentin antibody with immunofluorescence emission. Claim 8 is further drawn to claim 1, wherein the neoplastic cell is carcinoma cell.

Meschini et al., disclose a method of measuring a levels of cell surface expression of vimentin and comparing the level of vimentin protein in Multidrug resistant (MDR) neoplastic cells with non-resistant neoplastic cells to detect the MDR in neoplastic cells. Meschini et al., first disclose that drug resistant cells express MDR protein, p-glycoprotein, on the surface of the cells (page 620, page 4 and page 621, figure 5). Meschini et al., then, disclose that resistant cells display high level of surface vimentin, which is correlated with MDR protein expression, while the drug sensitive cells express no vimentin (page 619, figure 2). Meschini et al., disclose the expression of vimentin on the cell surface is determined by antibody to vimentin and measured by immunofluorescence emission (page 618 and 619, figure 2 and table II).

2. Claims 1-4 and 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Bichat et al., (Anticancer Res Treat, Vol 17, page 3393-3402, 1997)

Claims 1, 3-4, and 8 are set forth above. Claim 2 is further drawn to claim 1, wherein measuring the levels of cell surface expressed vimentin in the test neoplastic cells comprises isolating a cytoplasmic membrane fraction from the cells. Claims 6-9 are further drawn to claim 1, wherein the neoplastic cells are breast, carcinoma, or MCF7 cells, which are from breast tissue.

Bichat et al., disclose that over expression of vimentin is detected in the drug resistant breast cancer cells (MCF7R) compared to the nonresistant breast cancer (MCF7S). Bichat et al., disclose that vimentin expression is detected by immunodetection of cytoskeleton extract (including cytoplasmic membrane fraction) of the cells in Western blot (page, 3396, figure 2b). Bichat et al., also disclose the alteration of surface expression of vimentin is determined by antibody to vimentin and measuring by immunofluorescence emission (page 3397, table, and page 3398, figure 4).

3. Claims 59, 61-62 and 64-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Essa et al., (J of the Egyptian society of parasitology, vol 26, page 433-442, 1996) or Thomas et al., (Clinical Cancer Research, Vol 5, page 2698-2703).

Claim 59 is drawn to a method for detecting whether a test cells is neoplastic by surface expression of vimentin in a neoplastic cells comparing to the nonneoplastic cell, wherein the neoplastic cell has greater levels of vimentin expression compared to nonneoplastic cell. Claim 61 is further drawn to claim 59, wherein measuring the levels of cell surface expression vimentin in the test neoplastic cells by vimentin antibody. Claims 64-65 are further drawn to claim 59, wherein the neoplastic cell is carcinoma cell from breast tissue.

Essa et al., disclose a method of detecting the neoplasma cells in the breast carcinoma by vimentin expression. Essa et al., disclose that the expression of vimentin in the breast cancer cells is determined by immunohistochemistry with antibody to vimentin (page 436-437, figure 1-8). Essa et al., also disclose that vimentin is preferentially expressed in growing tumor cells and negative staining of

epithelial cells in non-neoplastic area (page 438, line 4-7 and paragraph 2).

Thomas et al., also disclose the vimentin expression in the breast cancer samples from breast cancer patients (page 2701, column 1, para 1). Thomas et al., disclose the method of detecing vimentin expression is determined by antibody for vimentin labeled with fluorescence dye (Rhodamine, figure 3, page 2701). Thomas et al., also disclose that the method can be used for diagnosis of breast pathology and poor prognosis (page 2699, column 1, line 12-13).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bichat et al., (Anticancer Res Treat, Vol 17, page 3393-3402, 1997) in view of Goldenberg et al., (US Patent, 4444744, 1984).

Claims 1-4 and 6-9 are set forth above. Claim 5 is further drawn to claim 3, wherein the antibody is radiolabeled.

Bichat et al., teach that over expression of vimentin is detected in the drug resistant breast cancer cells (MCF7R) compared to the nonresistant breast cancer (MCF7S,). Bichat et al., teach that vimentin is detected by immunodetection of cytoskeleton extract (including cytoplasmic membrane fraction) of the cells in Western blot (page, 3396, figure 2b). Bichat et al., also teach the alteration of surface expression of vimentin is determined by antibody to vimentin and measuring by immunofluorescence emission (page 3397, table, and page 3398, figure 4).

Bochat et al., do not teach measuring the level of antibody bound to cell surface vimentin by radiolabeled antibody.

Goldenberg et al., teach radiolabeled antibodies and method of making and using the antibody (column 10, line 61-68 example 5) and the use of these antibody to locate or diagnose the stage of tumors (column 14, example 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to detect MDR in breast cancer cells by detecting and comparing the vimentin expression in the cells to nonresistant cells using the antibody of the primary reference and measuring the protein with labeled antibody with radioactive material of secondary reference. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Bichat et al., to the teaching of Goldenberg et al et al., to use radiolabeled antibody to determine the expression of vimentin in the MDR breast cancer cells and compare the levels of vimentin in the resistant cells to non-resistant cells because Bichat et al., have shown a method of detecting of vimentin in MDR cancer cells by measuring the level of antibody bound to cell surface vimentin and Goldenberg et al., have shown a radiolabeled antibody for detection of its antigen.

2. Claims 59-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas et al., (Clinical Cancer Research, Vol 5, page 2698-2703).in view of Bichat et al., (Anticancer Res Treat, Vol 17, page 3393-3402, 1997) and Goldenberg et al., (US Patent, 4444744, 1984).

The claims 59, 61, and 64-65 are set forth above. Claim 60 is further drawn to claim 59, wherein the surface vimentin is in the cytoplasmic membrane fraction. Claims 62-63 are further drawn to claim 61, wherein the measuring the levels of antibody bound to the cell surface is by immunofluorescence emission and radiolabel.

The teaching by Thomas et al., set forth above.

Thomas et al., do not teach measuring vimentin expression in the test cell comprising isolating a cytoplasmic membrane fraction from the cell or bound the vimentin with radiolabeled antibody.

Bichat et al., teach detection of vimentin in cytoskeleton extract (including cytoplasmic membrane fraction) by Western blot (page, 3396, figure 2b).

Goldenberg et al., teach radiolabeled antibodies and method of making and using the antibody (column 10, line 61-68 example 5) and the use of these antibody to locate or diagnose the stage of tumors (column 14, example 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to measure the vimentin expression in test neoplastic cells by detecting and comparing the vimentin expression to nonneoplastic cells using the method and antibody of the primary reference and measuring the level of antibody bound to cell surface vimentin by immunofluorescence emission of secondary reference and measuring the vimentin with radiolabeled antibody of third reference. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Thomas et al., and Bichat et al., and Goldenberg et al., to measure the vimentin expression by immunofluorescence emission and/or radiolabeled antibody because Thomas et al., have shown how to detect a neoplastic cells by measuring the surface expression of vimentin, Bichat et al., have shown detecting the protein using antibody by in cytoskeleton extract (including cytoplasmic membrane fraction) by Western blot and Goldenberg et al., have shown a radiolabeled antibody and method of labeling the antibody with the radio-materials and method of using antibody for detecting its antigen.

3. Claims 10, 12 and 14-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bichat et al., (Anticancer Res Treat, Vol 17, page 3393-3402, 1997) in view of Heidenthal et al., (Biochem Biophys Res Comm, vol 267, page 49-53) and Fanger et al., (US Patent NO: 5762930, 1998).

Claim 10 is drawn to a method for detecting a MDR in a patient comprising administering to the patient, a vimentin binding agent. Claims 12 and 14 are further drawn to claim 10, wherein the vimentin binding agent is modified LDL labeled with fluorophores. Claims 15-19 are further drawn to claim 10, wherein the multidrug resistant cells is a breast cancer or breast epithelial resistant cells from human .

The teaching of Bichat et al.,on the alternation of surface vimentin by MDR breast cancer cells is set forth above.

Bichat et al., do not teach detecting MDR by administering a vimentin binding agent linked to a detectable agent, which bind to a surface-expressed vimentin in MDR cells.

Heidenthal et al., teach that binding of modified LDL to vimentin.

Fanger et al., teach that administering LDL to a patient, (column 3, para 1). Fanger et al., also teach the LDL is fluorophores-labeled or radio-labeled, which would bind to the cell expressing LDL binding protein on the surface (column 3 para 2 and column 11, para 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to detect the MDR cells from patient by measuring the administered vimentin binding agent, modified LDL. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Heidenthal et al., and Fanger et al., to Bichat et al., to detect the MDR cells detecting the vimentin binding agent, modified LDL, in the vimentin expression cells because Bichat et al., has shown that vimentin is expressed in the surface of MDR cells, Heidenthal et al., has shown that binding of modified LDL to vimentin and Fanger et al., has shown that administered labeled LDL, which binds to the cells expressing LDL binding protein.

4. Claims 66, 68 and 70-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Essa et al., (J of the Egyptian society of parasitology, vol 26, page 433-442, 1996) in view of Heidenthal et al., (Biochem Biophy res Comm (vol 267, page 49-53) and Fanger et al., (US Patent NO: 5762930, 1998).

Claim 66 is drawn to a method for detecting a neoplastic cell in a patient comprising administering to the patient, a vimentin binding agent, modificed LDL, linked to a detectable label. Claims 68 and 70 are further drawn to claim 66, wherein the vimentin binding agent is modified LDL labeled with fluorophores. Claims 71-74 are further drawn to claim 66, wherein the neoplastic cell is breast cancer cells or breast cancer epithelial cell from patient suffering from a disorder caused by the presence of the neoplastic cell.

The teaching of Essa et al., on the expression of vimentin by breast cancer cell and nonneoplastic cells is set forth above.

Essa et al., do not teach detecting neoplastic cell in the patient by administering a vimentin binding agent, modified LDL, linked to a detectable label.

Heidenthal et al., teach that binding of modified LDL to vimentin.

Fanger et al., teach that administering LDL to a patient, (column 3, para 1). Fanger et al., also teach the LDL is fluorphores- or radio-labeled, which would bind to a cell expressing LDL binding protein on the surface (column 3, para 2 and column 11, para 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to detect the MDR cells from patient by measuring the administered vimentin binding agent, modified LDL. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Heidenthal et al., and Fanger et al., to teaching of Essa et al., to detect the neoplastic cell by detecting the vimentin binding agent, modified LDL, in the vimentin expression cells because Essa et al., has shown that vimentin is expressed in the neoplastic cell, Heidenthal et al., has shown that binding of modified LDL to vimentin, and Fanger et al., has shown that administered labeled LDL, which binds to the cells expressing LDL binding protein..

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner

SHEELA HUFF
PRIMARY EXAMINER